In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 18-1885V
Filed: March 12, 2024

JEFFREY COOPER,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Special Master Horner

Ronald C. Homer, Conway, Homer, P.C., Boston, MA, for petitioner.
Parisa Tabassian, U.S. Department of Justice, Washington, DC, for respondent.

Ruling on Entitlement[1]

On December 7, 2018, petitioner, Jeffrey Cooper, filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10, *et seq.* (2012),[2] alleging that he suffered Guillain-Barrè Syndrome ("GBS") caused-in-fact by his pneumococcal 13-valent conjugate ("Prevnar 13") vaccination, which he received on June 29, 2017. (ECF No. 1.) For the reasons set forth below, I conclude that petitioner is entitled to an award of compensation.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute;

[1] Because this document contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the document will be available to anyone with access to the internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] Within this ruling, all citations to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(A); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991). Although GBS is a Table Injury relative to the influenza ("flu") vaccine, it is not a Table Injury for the pneumococcal conjugate vaccine. 42 C.F.R. § 100.3. Accordingly, petitioner must meet the burden of proof for an injury caused-in-fact by vaccination.

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause of the injury or condition but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" the logical sequence must be supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine.

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting her causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. That expert's opinion must be "sound and reliable." *Boatmon v. Sec'y of Health & Human Servs*., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019) (citing *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548-49 (Fed. Cir. 1994)). The *Althen* court also indicated, however, that a Program fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." 418 F.3d at 1280.

Generally, respondent bears the burden of demonstrating the presence of any alternative cause by preponderant evidence only if petitioner satisfies her *prima facie* burden. § 300aa-13(a)(1)(B); *Walther v. Sec'y of Health & Human Servs*., 485 F.3d 1146, 1150 (Fed. Cir. 2007). However, respondent may also present evidence relating to an alternative cause to demonstrate the inadequacy of petitioner's evidence supporting her case in chief. Nonetheless, petitioner does not bear the burden of eliminating alternative causes where the other evidence on causation is sufficient to establish a *prima facie* case under *Althen*. *de Bazan v. Sec'y of Health & Human Servs*., 539 F.3d 1347, 1352-53 (Fed. Cir. 2008); *Walther*, 485 F.3d at 1150.

II. Procedural History

On December 7, 2018, petitioner filed his petition alleging that the Prevnar 13 vaccination he received on July 13, 2016, caused-in-fact his Guillain Barré syndrome ("GBS"). (ECF No. 1.) This case was originally assigned to Special Master Sanders. (ECF No. 4.) Petitioner filed his affidavit and medical records between December 2018 and July 2019. (ECF Nos. 8-11; 17, 19.) The case was reassigned to my docket in August of 2019. (ECF Nos. 24-25.)

Petitioner filed updated medical records in September of 2019 and respondent filed his Rule 4 (c) Report the following December. (ECF Nos. 26, 30.) Respondent argued that the evidence presented did not meet petitioner's burden and recommending against compensation. (ECF No. 30.) Respondent stressed that petitioner developed GBS too long after vaccination to support his claim, as he informed his treating

physicians that his first symptoms began on August 28, 2017, or approximately 8.5 weeks post vaccination. (*Id.* at 6-7.) Moreover, respondent urged that petitioner had not demonstrated a reliable theory for how the Prevnar vaccine can cause GBS. (*Id.* at 6.)

Petitioner then filed an expert report from neurologist Norman Latov, M.D., Ph.D., in February of 2020. (ECF No. 32, Ex. 23.) In May of 2020, respondent filed a responsive expert report from neurologist Brian Callaghan, M.D. (ECF No. 36, Ex. A.) Subsequently, the parties exchanged three further rounds of supplemental expert reports. (*See* Exs. 41, 46, 56; Exs. G-I.) An entitlement hearing was held remotely on January 18th, 2023, via Zoom. (*See* ECF No. 90, Transcript of Proceedings ("Tr."), filed Feb. 3, 2023.) Petitioner and the parties' respective experts testified.

This case is now ripe for resolution of entitlement.

III. Factual History

a. As reflected in the medical records

Petitioner's past medical history includes coronary artery disease, obstructive sleep apnea, hypertension, hyperlipidemia, and benign prostatic hyperplasia with nocturia. (*See* Ex. 3, pp. 2-4.) On June 29, 2017, petitioner received the Prevnar 13 vaccine. (Ex. 1.) On August 11, 2017, petitioner presented to his primary care physician ("PCP") for follow-up for his coronary artery disease and sleep apnea. (Ex. 3, pp. 7-11.) Petitioner's physical examination was normal, and he was counseled about his high body mass index. (*Id.* at 10.) Petitioner did not mention experiencing any tingling or weakness at this appointment.

On September 4, 2017, petitioner presented to the emergency room with complaints of progressive muscle cramping in his feet, as well as rising tingling and numbness beginning around August 31, 2017. (Ex. 12, pp. 23-26.) He reported decreased dexterity in his hands, trouble knowing when to use the bathroom (no feeling of urgency), abdominal distention, and shortness of breath. (*Id.* at 24.) Petitioner further reported a history of sleep apnea and a recent inability to wear his CPAP machine due to rib pain. (*Id.*) He reported falling twice as a result of the progressive weakness. (*Id.*) Petitioner explained that he noticed the symptoms getting worse on September 1, 2017, when he noticed that his legs were feeling "very heavy" during a regular walk with his wife. (*Id.* at 25.) He described a gradual onset of these symptoms. (*Id.)* On physical examination, petitioner showed reduced deep tendon reflexes in his lower extremities. (*Id.* at 26.) He also had an elevated CSF protein with normal CSF white blood cell count. (*Id.*)

Petitioner was admitted that same day. (Ex. 12, pp. 9-12.) Lhissa Natalia Santana, M.D., examined petitioner and noted that he had no diarrhea, flu-like symptoms, tick exposure, or sick contacts, and that "[t]he only risk factor that he has, he had [two] vaccines done in May and June respectively. He had shingles vaccine and

pneumonia vaccine. That is the only risk factor that he had." (*Id.* at 10.) Petitioner denied nausea, vomiting, diaphoresis, chest, pain, and shortness of breath. (*Id.*) Dr. Santana assessed petitioner with progressive weakness associated with negative deep tendon reflexes and with albumin of cytologic dissociation in the lumbar puncture, which is consistent with GBS. (*Id.* at 11.) Dr. Santana started petitioner on IVIG for five days. (*Id.*)

On September 6, 2017, petitioner underwent an electromyogram/nerve conduction study ("EMG/NCS"). (Ex. 12, pp. 13-14.) The study revealed evidence of polyneuropathy demyelination, which could be explained by early GBS. (*Id.* at 14.) Most of the findings were fairly mild, and there was no evidence of cervical or lumbar radiculopathy. (*Id.*) That same day, petitioner presented to neurologist, Bret Warner, M.D., for a consultation. (*Id.* at 17-19.) On examination, petitioner demonstrated decreased grip strengths bilaterally and some decreased plantar and dorsiflexion of the ankles bilaterally, although his muscles appeared to be otherwise intact. (*Id.* at 18.) Petitioner also had absent knee and ankle reflexes bilaterally and trace reflexes at the biceps and triceps in the upper extremities bilaterally. (*Id.*) His sensory examination appeared to be intact. (*Id.*) Dr. Warner questioned whether petitioner had some decreased fine touch in both feet. (*Id.*) He concluded, "[a]ll of this would fit the clinical diagnosis of [GBS]." (*Id.*)

On September 9, 2017, petitioner was discharged to inpatient rehabilitation with the following diagnoses: GBS, abdominal pain, upper back pain, hyperlipidemia, and benign prostate hypertrophy. (Ex. 12, p. 20.) Although he was still complaining of paresthesia in his fingertips and toes, petitioner was experiencing improvements in his strength and sensation. (*Id.* at 20-22.) Petitioner reported abdominal pain and Dr. Warner questioned whether it was caused by his GBS, but petitioner's imaging results and physical examination were unremarkable. (*Id.* at 21.) Petitioner was also believed to be constipated as a result of not eating or drinking enough. (*Id.*)

On the same day, petitioner was admitted to Greenwood Regional Rehabilitation Hospital. (Ex. 13, p. 1.) The admission notes indicate that he responded well to IVIG, with improvement in his lower extremities; however, he reported some numbness in his lips and difficulty swallowing. (*Id.* at 176-77.) On examination, petitioner's patellar reflexes were absent, though he demonstrated reflexes in his forearm that were "brisk." (*Id.* at 177.) He was also observed to have facial paralysis. (*Id*.) The next day, on September 11, 2017, Jonathan Hegler, M.D., noted petitioner likely had the acute inflammatory demyelinating polyradiculoneuropathy ("AIDP") variant of GBS because "he is experiencing the treatment related fluctuation often typical after initial treatment." (*Id.* at 179-80.) On September 12, 2017, petitioner underwent a brain MRI, which revealed a "[f]ocus of low volume subcortical frontal white matter hemosiderin signal" that was "believed to be related to a prior old subcortical microhemorrhage in the past" and was similar to "findings seen in the am upper left cerebellum." (Ex. 12, pp. 64-65.) The MRI results also noted "[m]ild patient motion" and "[o]therwise normal MR head." (*Id.* at 65.) Dr. Hegler concluded that these findings were nonspecific and "not responsible for what he [was] experiencing." (Ex. 13, p. 192.) By September 13, 2017,

Dr. Hegler believed petitioner's deterioration had stopped. (*Id.*) He believed that petitioner's presentation involved an autonomic component, in addition to the treatment related fluctuation, as evidenced by his tachycardia and the atonic colon. (*Id.*)

Petitioner attended inpatient speech, occupational, and physical therapies throughout the month of September 2017. (Ex. 13, pp. 466-519.) On September 16, 2017, David Bridges, M.D., noted petitioner continued to suffer "lower extremity weakness that has not really resolved and retained upper extremity strength with some facial tingling which is now improving this morning." (*Id.* at 188.) Dr. Bridges recorded that "[t]here was no antecedent viral illness though he did have immunizations a good bit of time before he had trouble with his motor weakness." (*Id*.) By September 27, 2017, petitioner's upper extremity and thigh strength had significantly improved. (*Id.* at 211.) Petitioner was now walking with a rolling walker. (*Id.*) Petitioner continued inpatient speech, occupational, and physical therapies until October 4, 2017. (*Id.* at 520-29.)

On October 6, 2017, petitioner was discharged home from inpatient rehabilitation by Clifford Monda, D.O. (Ex. 13, pp. 128-30.) Dr. Monda noted that petitioner initially injured himself while pushing a boat into the water, during which he felt a pull on the left side of his ribs followed by pain in his back. (*Id.* at 128.) Although, Dr. Monda felt this was a "separate issue" because petitioner began feeling numbness in his toes and ankles and progressive weakness "multiple days later." (*Id.*) Dr. Monda noted that petitioner received shingles and pneumonia vaccines in May and June 2017, "but had been doing great after those vaccines without any problems." (*Id.*) Petitioner responded well to IVIG, though he felt his lower extremities were still improving and he complained of a new symptom of lip numbness. (*Id.* at 129.) He indicated the lip numbness made it difficult to talk and swallow. (*Id.*) Petitioner's biggest complaint throughout his stay was continued low back pain, for which was started on low-dose OxyContin. (*Id.*) He was given a lumbar sacral orthosis (LSO) brace at the time of discharge. (*Id.*)

Petitioner followed-up with Dr. Warner on October 9, 2017. (Ex. 10, pp. 16-17.) During this appointment, petitioner complained of facial numbness and left leg weakness. (*Id.* at 16.) Petitioner was now able to walk with either a walker or a quad cane, though he was experiencing some paresthesia. (*Id.*) His neurological examination revealed weak dorsiflexion in both ankles, mild decrease in sensory vibration, and absent deep tendon reflexes in both lower extremities and trace deep tendon reflexes in the upper extremities. (*Id.*) Dr. Warner ordered an updated nerve conduction study and lumbar spine MRI to investigate possible spinal stenosis. (*Id.* at 17.) Petitioner was restarted on Crestor, which he took to control his cholesterol and had stopped taking while he was being treated in the hospital. (*Id.* at 17-18.)

Petitioner had a follow up appointment with his PCP on October 17, 2017, during which she noted petitioner was improving with physical, occupational, and speech therapy services working with him at home. (Ex. 3, pp. 15-16.) Petitioner had graduated from using a walker to a four-point walking cane, but he still had left-sided

weakness and facial drooping, as well as continued difficulty with his speech and swallowing. (*Id.* at 16.) The EMG/NCV studies performed on October 18, 2017, revealed sensory polyneuropathy and demyelination, and remained unchanged from the study performed on September 6, 2017. (Ex. 10, p. 10.)

Petitioner continued speech, physical, and occupational therapies at home throughout October, November, and December 2017 and he was discharged from these services by early January 2018. (Ex. 14, pp. 138-370.) Petitioner returned to his PCP on November 7, 2017, who reported that he was progressing well with rehabilitation. (Ex. 2, pp. 3-4.) He reported that petitioner's treaters did not know what had caused his GBS, however, they suspected his Prevnar 13 vaccine or Crestor medication. (*Id*.) As a result, his neurologist had changed his medication to Lipitor. (*Id.*) Prevnar 13 and Pneumovax 23 were listed under the allergies and adverse drug reactions section of the report for this visit. (*Id.* at 4.) On January 11, 2018, petitioner reported to the emergency room with suspected influenza. (Ex. 12, pp. 75-79.) His PCP prescribed him Tamiflu because of his history of GBS. (*Id*. at 79.)

On March 12, 2018, petitioner followed-up with his neurologist Dr. Warner. (Ex. 10, pp. 8-9.) On examination, petitioner exhibited weak dorsiflexion of both ankles, diminished sensation and absent deep tendon reflexes in his legs and arms, and a slow and broad-based gait. (*Id*. at 8.) An EMG/NCV study still revealed mild polyneuropathy but showed improvement from the previous study. (*Id.* at 4-6.)

On May 2, 2018, petitioner returned to Dr. Warner, showing further signs of improvement. (Ex. 10, pp. 2-3.) He was regaining sensation in his face, and his paresthesia was mild. (*Id.*) However, petitioner complained of two episodes of confusion, describing how he was not certain what he was doing for several minutes. (*Id.* at 2.) Dr. Warner ordered a brain MRI, with and without contrast, to investigate possible cerebrovascular disease. (*Id.* at 3.) Petitioner underwent the brain MRI on May 23, 2018, the results of which were "[e]ssentially unremarkable." (*Id.* at 1.) An EMG/NCV performed on June 19, 2019, was normal with no evidence of electrical instability in any of the examined muscles. (Ex. 19, p. 1.)

Petitioner presented to Dr. Warner again on June 21 and October 2, 2018. (Ex. 19, pp. 15-18.) Dr. Warner noted that petitioner improved, though he continued to have fatigable weakness and mild paresthesia, with aching sensations in his legs after walking. (*Id.*) On October 10, 2018, petitioner underwent repeat EMG/NCS studies. (*Id.* at 10-14.) The findings revealed decreased conduction velocity in the right ulnar motor nerve, while all remaining nerves were within normal limits. (*Id.* at 10.) All examined muscles were showed no evidence of electrical instability. (*Id.*)

On January 16, 2019, petitioner returned to Dr. Warner complaining of aching sensations in his legs, and mild twitching on the left side of his face that "comes and goes." (Ex. 19, pp. 8-9.) On examination, petitioner demonstrated 5/5 strength throughout, with normal bulk and tone; mild decrease in sensory vibration; absent deep tendon reflexes in both lower extremities and trace deep tendon reflexes in the upper

extremities; and a slow and broad-based gait. (*Id.* at 8.) In June 2019, petitioner complained that he could not fully raise his upper lip, making it difficult to brush his teeth. (*Id.* at 6.) He also complained of shortness of breath with any sort of exercise. (*Id.*) Petitioner underwent repeat EMG/NCS on June 19, 2019, which revealed normal findings. (*Id.* at 1-5.)

On September 30, 2019, petitioner was referred to neurologist Jerry Pruitt, M.D., at the request of his PCP. (Ex. 78, p. 20.) Petitioner indicated his belief that his GBS "was potentially caused by a pneumococcal vaccine that he received within a few prior [*sic*] to s[ymptom] onset." (*Id.*) Petitioner reported beginning amantadine two to three months prior and noticed a reduction in leg aches, fasciculations, and weakness. (*Id.* at 21.) However, he began to experience blurry peripheral vision, which he believed to be a side effect. (*Id.*) He also reportedly resumed his usual walk. (*Id.*) However, petitioner reported residual facial weakness (worse on the left) and bilateral lower extremities weakness (also worse on the left). (*Id.*) Dr. Pruitt reported in her impression of petitioner that he had a history of chronic inflammatory demyelinating polyneuropathy ("CIDP") but noted that petitioner's new symptoms were possibly consistent with a disorder of neuromuscular transmission.[3] (*Id.* at 22-23.) Dr. Pruitt ordered labs and nerve conduction studies. (*Id.* at 23.) On April 17, 2020, Dr. Pruitt noted that petitioner's nerve conduction study and single-fiber electromyography[4] were both negative for neuromuscular junction disorder and his AchR antibody levels were zero. (*Id.* at 7-8.) He concluded petitioner's current symptoms were residual from his 2017 GBS and not represent neuromuscular junction disorder. (*Id.* at 7.) Still, he ordered a trial of Mestinon to treat petitioner's current symptoms. (*Id.*)

On September 16, 2020, petitioner established care with a new neurologist, John Baker, M.D. (Ex. 72, p. 24.) Petitioner complained of residual symptoms, including vision changes in his left eye; difficulty eating; shaking and cramps in his face; cramping and aching in his thighs, calves, and toes; and exertional weakness. (*Id.*) Petitioner's neurological exam was normal except for ptosis in both eyes, fatigable weakness, and 4/5 motor strength and tone in his upper and lower extremities. (*Id.* at 25.) Dr. Baker assessed petitioner with, in pertinent part, weakness and GBS. (*Id.*) He noted that petitioner had an underlying CIDP variant of GBS with facial and oculomotor involvement and fixed nerve injury that fluctuates day to day. (*Id.*) He further indicated that petitioner had a neuromuscular junction disorder "underlying all this time." (*Id.*) Dr. Baker considered treating petitioner with IVIG and prednisone. (*Id.*) In October 2020,

[3] In his prehearing brief, respondent noted that some of petitioner's later medical records suspected petitioner's condition might be better characterized by CIDP rather than GBS. He reserved the right to challenge diagnosis during the hearing. (ECF No. 86, n. 3.) However, during the hearing his expert endorsed the GBS diagnosis. (Tr. 129-30.)

[4] A Single-fiber electromyography (SFEMG) uses a needle extrude to record the action potential of one muscle fiber at a time. *Single-fiber electromyography*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=72662 (last visited Dec. 8, 2023).

Dr. Baker assessed petitioner with Myasthenia gravis[5] and restless leg syndrome. (*Id.* at 23.)

Petitioner presented to Dr. Baker again in December, 2020, and June, 2021. (Ex. 72, pp. 18-21.) Petitioner reported reduced leg cramping with Mirapex, but residual achiness. (*Id.*) He further reported ongoing facial weakness. (*Id.* at 18.) On July 16, 2021, petitioner underwent lumbar spine MRI without contrast. (*Id.* at 17.)

Approximately one year later, on August 17, 2022, petitioner presented for a follow-up visit regarding his weakness, after having been sick in June with respiratory symptoms and weakness. (Ex. 72, pp. 13-14; Ex. 77, pp. 4-6.) Petitioner's neurological exam was unremarkable. (Ex. 72, p. 13.) Dr. Baker ordered refills for petitioner's medications, including Mirapex and Mestinon. (*Id.* at 14.) No further records were filed.

b. Petitioner's affidavit and testimony

Petitioner's testimony and affidavit were largely consistent. (Ex. 16; Tr. 5-45.) Petitioner testified that he had high cholesterol and an enlarged prostate before his vaccinations but was otherwise healthy. (Tr. 7.) He explained that he kept a log that tracked his daily exercise. (*Id.* at 8.) In August 2017, he pulled his rib while attempting to put his pontoon boat in the water. (*Id.* at 9-11.) He later began to notice some unusual tiredness in his legs after activity. (*Id.*) For example, he described exhaustion and heaviness in his legs after a long drive. (*Id.* at 10-11, 43-44.) He described how his condition progressed and walking became much harder, and he noticed achiness in his legs and tingling in his hands and feet. (*Id.* 9-10.) When he walked again after resting for a couple of days, he could barely lift his legs. (*Id.* at 10-11.)

In early September 2017, petitioner attempted a long drive that left his legs feeling exhausted. (Tr. 13-14.) He needed to rest for the remainder of the day. (*Id.* at 14.) The following day, his legs were "more and more tired" and the tingling had intensified. (*Id.*) He testified that he stayed on the couch the entire day. (*Id.*) He described how he attempted to get off the couch only to fall to the floor. (*Id.*) Although he was able to stand up afterwards, petitioner explained that he needed to lean against the wall to walk. (*Id.* at 14-15.) When he returned to the couch, he fell again. (*Id.*) He went to the hospital the following day. (*Id.* at 15.)

Petitioner explained that his current condition is one of "diminished ability." (Tr. 26.) He still suffers from facial palsy that worsens with tiredness and experiences tingling in his hands and feet. (*Id.* at 26-29.) He is no longer about walk or stand for long periods of time. (*Id.* at 27-28.) He explained, "I basically had a half of a day.

[5] Myasthenia gravis is an autoimmune disease of neuromuscular function due to the presence of antibodies to acetylcholine receptors at the neuromuscular junction. *Myasthenia gravis*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=91080 (last visited Nov. 21, 2023). It may be restricted to a single muscle group, especially the muscles of the eyes, fact, lips, tongue, throat, and neck, or it make become generalized with severe weakness and sometimes respiratory insufficiency. *Id.* Symptoms of myasthenia gravis include muscle fatigue and exhaustion that fluctuates in severity but without sensory disturbance or atrophy. *Id.*

That's all I have. . . . I pretty much will only have any activity for half a day . . . ." (*Id.* at 28.) He can no longer travel with his wife or swing a golf club. (*Id.* at 30-31.) Due to his lack of balance and strength, he is no longer able to ride his bike like he once could. (*Id.* at 31.) He further explained that he used to love walking on the beach, but walking on the beach is no longer feasible because "you've got to pick up your legs." (*Id.* at 32.)

On cross-examination, petitioner clarified that his hospitalizations and rehab were not specifically related to his GBS and that he was not attributing his back pain to his GBS, though it was occurring simultaneously. (Tr. 40-42.) He further clarified his medical records that reported tingling in his ankles, explaining that the sensation started in his feet and traveling "up through his ankles." (*Id.* at 38.) Petitioner explained that the records noting tingling in his ankles and heels are consistent with his testimony that the tingling was in his feet "entirely," rather than limited to a specific portion of his feet. (*Id.* at 38-39.) Although he resumed his daily walking regimen, petitioner stated that he walks at a slower pace and for much shorter distances. (*Id.* at 42.)

IV. Summary of Expert Opinions

a. Petitioner's Expert, Norman Latov, M.D., Ph.D.

Dr. Norman Latov submitted four expert reports and testified in this case, without objection, as an expert in neurology and neuroimmunology.[6] (Ex. 23, 41, 46, 56; Tr. 50.) He opines to a reasonable degree of medical certainty that petitioner suffered GBS which was caused by his June 29, 2017 Prevnar 13 pneumococcal vaccine. (Ex. 23, p. 3.)

Dr. Latov explains that GBS, or Acute Inflammatory Demyelinating Polyneuropathy (AIDP), is an autoimmune condition that acutely affects the peripheral nerves. (*Id.*) Typical symptoms include weakness and sensory loss in the limbs and less often the chest or face. (*Id*.) He notes that GBS is well known to follow both infection and vaccination. (*Id.* (citing Eitan Israeli et al., *Guillain-Barré Syndrome–A Classical Autoimmune Disease Triggered by Infection or Vaccination*, 42 CLIN. REV. ALLERGY IMMUNOL. 121 (2012) (Ex. 30)); Tr. 53-54.) Two vaccines in particular, an anti-rabies vaccine and the 1976 swine flu vaccine, have been shown to result increased incidences of GBS. (Ex. 23, p. 3 (citing Emanuel Applebaum et al., *Neurological*

[6] Dr. Latov received his medical degree and Ph.D. in pathology from the University of Pennsylvania School of Medicine. (Ex. 24, p. 1.) He completed his residency in neurology at the Neurological Institute at Columbian Presbyterian Medical Center in New York. (*Id.* at 2.) Following his residency, Dr. Latov completed a fellowship in immunology and through 2012 headed a laboratory of neuroimmunology that conducted research into the mechanism of autoimmune peripheral neuropathies. (Ex. 23, p. 1.) The laboratory is credited with the discovery of anti-MAG and GM1 ganglioside antibodies, and development of assays that are currently used for testing patients with suspected autoimmune neuropathies. (*Id.*) Dr. Latov has published over 200 articles related to autoimmune neuropathies in peer-reviewed journals. (*Id.*; Ex. 24, pp. 3-17.) Dr. Latov is board certified in neurology and has devoted a substantial portion of his practice to the evaluation, diagnosis and treatment of patients with autoimmune neurological diseases, including GBS. (Ex. 23, pp. 1.) He currently serves as a professor of neurology and neuroscience at the Weill Medical College at Cornell University. (Ex. 24, p. 2.)

Complications Following Antirabies Vaccination, 151 J. AM. MED. ASS'N 188 (1953) (Ex. 25); Lawrence Schonberger et al., *Guillain-Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977,* 110 AM. J. EPIDEMIOLOGY 105 (1979) (Ex. 33)).) Dr. Latov further suggests that GBS has been observed to follow both pneumonia infection[7] and pneumonia vaccination.[8] (*Id.* at 4.) Regarding an overall lack of available epidemiology, Dr. Latov cautions that while the flu vaccine is administered annually, the pneumococcal vaccine is administered only once after the age of 65. (Ex. 41, p. 1.)

In petitioner's case, Dr. Latov observes that GBS developed "approximately eight weeks"[9] post-vaccination. (Ex. 23, p. 5.) According to Dr. Latov, this is within the time period of elevated risk for developing GBS post-vaccination. (*Id.*) To support this conclusion, Dr. Latov cites a study by Schonberger et al., that examined incidences of GBS following a 1976 program for vaccination against the swine flu. (*Id*. (citing Schonberger et al., *supra*, at Ex. 33).) That study found that most post-vaccination GBS cases occurred within five weeks of vaccination, but also observed an increased risk lasting up to nine or ten weeks. (*Id*.) Although respondent's expert cited a follow up study, by Langmuir et al., that found a reduced risk period of eight weeks and no longer, Dr. Latov finds the Schonberger analysis to be more scientifically sound, disagreeing with the Langmuir study's case selection criteria and noting that the study nonetheless still observed increased incidences of GBS in weeks nine and ten post-vaccination. (Ex. 41, pp. 2-3 (discussing Alexander Langmuir et al., *An Epidemiologic and Clinical Evaluation of Guillain Barré Syndrome Reported in Association with the Administration of Swine Influenza Vaccines,* 119 AM. J. HYGIENE 841 (1984) (Ex. 43; also filed as Ex. E)).) Dr. Latov further stresses that no other cause for petitioner's condition was identified, *i.e.* there was no preceding infection or other possible trigger, and his treating physicians identified his vaccination as the "only risk factor he had." (Ex. 23, p. 5 (quoting Ex. 12, p. 10).)

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[7] Notably, however, Dr. Latov's source for this assertion, Israel, et al., cites prior experience with GBS following mycoplasma pneumoniae (m. pneumoniae) (Israeli, et al., *supra*, at Ex. 30, p. 3) whereas the Prevnar vaccine prevents streptococcus pneumoniae (s. pneumoniae) (Hung Fu Tseng et al., *Pneumococcal Conjugate Vaccine Safety in Elderly Adults*, 5 OPEN F. INFECTIOUS DIS. (2018) (Ex. 37)).

[8] For this point Dr. Latov cites a case report: Nidhi Ravishankar, *Guillain-Barré Syndrome Following PCV Vaccine,* 2 CLINICS SURGERY 1413 (2017) (Ex. 32). He also cites data collected from the Vaccine Adverse Event Reporting System (VAERS). (*See* Exs. 39, 45.) Further to that, he references Tseng, et al., *supra*, at Ex. 37. The Tseng study compared the rates of adverse events following the pneumococcal conjugate vaccine, as at issue in this case, to the earlier pneumococcal polysaccharide vaccine. (*Id.*) The study found no increased rate of adverse events from the conjugate vaccine compared against the polysaccharide vaccine. (*Id.*) However, looking at the study's data for GBS, Dr. Latov observes that the total number of cases observed by the study is higher than the known background rate of GBS among the population. (Tr. 62-65 (discussing Ex. 37, p. 6 (table 3).) Respondent's expert, Dr. Callaghan, agreed that Dr. Latov is correct to observe that the raw numbers show above-background incidences of GBS, but cautions that it is a small number, lacks any finding of statistical significance, and is based on a questionable grouping of cases following both the conjugate and polysaccharide vaccines. (*Id.* at 162-63.)

[9] 60 days, or eight weeks and four days, to be precise. (Tr. 104.)

To explain how the Prevnar vaccine can cause GBS, Dr. Latov endorses two mechanisms that have been accepted by the Institute of Medicine ("IOM")[10] as possible explanations for post-vaccination adverse events – molecular mimicry and bystander activation. (Ex. 23, p. 4 (citing INSTITUTE OF MEDICINE, ADVERSE EFFECTS OF VACCINES: EVIDENCE AND CAUSALITY 57 (Stratton et al. eds., 2012) [hereinafter 2012 IOM Report] (Ex. 29)).) By Dr. Latov's description "[m]olecular mimicry occurs when there is a structural homology, due to sequence or conformation, between an exogenous agent, such as a vaccine or infection, and a self or autoantigen that is subsequently targeted. Induction of immune reactivity against the foreign agent results in cross reactivity with the self-antigen, with subsequent tissue damage and autoimmune disease." (*Id*.) Molecular mimicry can often involve amino acid or protein sequences, but also other molecular structures such as lipids and sugars. (Tr. 98-99.) Regarding bystander activation, he observes that the normal immune state incudes auto-reactive cells that are suppressed by immune tolerance, thereby preventing autoimmune disease. Bystander activation occurs when infection or immunization stimulate the immune system in such a way as to overcome that immune tolerance. (Ex. 23, p. 4.) Dr. Latov explains that these two mechanisms, bystander activation and molecular mimicry, can operate either independently or in conjunction. (Tr. 60-61.)

Molecular mimicry is an accepted cause of GBS insofar as cross reaction resulting from homology between the *Campylobacter jejuni* bacterium and gangliosides within the peripheral nerves has been shown to result in the Acute Motor Axonal Neuropathy (AMAN) type of GBS. (Ex. 23, p. 4 (citing Maojun Zhang et al., *Association Study Between an Outbreak of Guillain Barré Syndrome in Jilin, China, and Preceding* Campylobacter jujni *Infection,* 7 FOODBORNE PATHOGENS & DISEASE 913 (2010) (Ex. 40)); Tr. 57-61.) According to Dr. Latov, animal model studies involving experimental allergic neuritis (EAN) have also shown that molecular mimicry can likewise result in the demyelinating form of the condition. (Ex. 23, p. 4 (citing Betty Soliven, *Animal Models*

[10] The Institute of Medicine (known as the National Academy of Medicine since 2015) is the medical arm of the National Academy of Sciences. The National Academy of Sciences ("NAS") was created by Congress in 1863 to be an advisor to the federal government on scientific and technical matters (*see* An Act to Incorporate the National Academy of Sciences, ch. 111, 12 Stat. 806 (1863)), and the Institute of Medicine is an offshoot of the NAS established in 1970 to provide advice concerning medical issues. When it enacted the Vaccine Act in 1986, Congress directed that the IOM conduct studies concerning potential causal relationships between vaccines and illnesses. *See* § 300aa–1. However, the IOM employs a standard for finding causation that is higher than what is required by petitioner's burden of proof. *E.g. Raymo v. Sec'y of Health & Human Servs.*, No. 11-654V, 2014 WL 1092274, at *21, n. 39 (Fed. Cl. Spec. Mstr. Feb. 24, 2014). Accordingly, IOM reports and findings should be approached with caution. Special Masters may rely on IOM reports as evidence, but they are not dispositive. *See, e.g., Crutchfield v. Sec'y Health & Human Servs.*, 125 Fed. Cl. 251, 262 (2014) (noting that "it was appropriate for the special master to consider the medical literature presented, including the IOM report" and that "the court often has relied on the findings of the Institute of Medicine."); *see also, Isaac v. Sec'y Health & Human Servs.,* 108 Fed. Cl. 743, 755 (2013), *aff'd,* 540 Fed. Appx. 999 (Mem.) (Fed. Cir. 2013) (affirming the special master's reliance on findings of the IOM); *Porter v. Sec'y Health & Human Servs.,* 663 F.3d 1242, 1252 (Fed.Cir.2011) (noting the special master's comment that "IOM reports are favored, although not dispositive, in the Vaccine Act Program," then affirming the special master's decision).

of Autoimmune Neuropathy, 54 INST. LAB'Y ANIMAL RSCH. 282 (2013) (Ex. 34)).) Experimental allergic encephalomyelitis (EAE) studies have also shown that bystander activation can likewise play a role in autoimmune demyelination. For example, Dr. Latov cites a study by Goverman et al., in which mice that expressed myelin basic protein-specific T cells did not develop EAE unless also exposed to an immune stimulant. (*Id*. (citing Joan Goverman et al., *Transgenic Mice That Express a Myelin Basic Protein-Specific T Cell Receptor Develop Spontaneous Autoimmunity,* 72 CELL 551 (1993) (Ex. 28)).)[11] Dr. Latov notes that the Prevnar vaccine includes a modified diphtheria toxin protein (CRM197) that provides an adjuvant T-cell response. (Ex. 41, p. 2 (citing Henry R. Shinefield, *Overview of the Development and Current Use of CRM$_{197}$ Conjugate Vaccines for Pediatric Use,* 28 VACCINE 4335 (2010) (Ex. 44)).) Thus, he opines it is reasonable to invoke bystander activation relative to the Prevnar vaccine in the context of GBS. (*Id*. (citing Goverman et al., *supra*, at Ex. 28).)

Dr. Latov acknowledges there are no studies examining whether the Prevnar vaccine cross reacts with normal human tissue. (Ex. 41, p. 2.) However, Dr. Latov proposed three different homologies between the Prevnar vaccine and myelin tissue that he posited can substantiate his reliance on molecular mimicry. (Exs. 46, 56.) Ultimately, during the hearing, he presented two. (Tr. 69-80.) Because I have concluded for the reasons discussed below, that one of those theories is preponderantly supported, I will not address the other two theories.[12]

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[11] Dr. Callaghan is critical of Dr. Latov's citations to EAE studies. He suggests "the connection from EAE, which is an experimental model of multiple sclerosis, to GBS is . . . unclear." (Ex. G, p. 1.) Dr. Callaghan's point is well taken insofar as EAN is a widely accepted model for peripheral nervous system conditions such GBS (Soliven, *supra,* at Ex. 34, p. 2) whereas EAE is a central nervous system counterpart. (Hugh J. Willison, *Glycoconjugates and Neuroimmunological Diseases, in* ADVANCED NEUROBIOLOGY 543, 545-46 (R.K. Yu & C.L. Schengrund eds., 2014) (Ex. 38, pp. 3-4).) However, Dr. Callaghan overstates the case to the extent he characterizes EAE as being viewed solely as a model for multiple sclerosis. For example, while the Goverman, et al., study notes its particular potential for studying multiple sclerosis, it also characterizes its findings as providing insights for demyelinating autoimmune disease more broadly. (Goverman et al., *supra,* at Ex. 28, p. 8.) Likewise, the IOM, relied on by Dr. Callaghan, cites a rabbit model of "EAE-like disease" among findings applicable to demyelinating diseases broadly. (2012 IOM Report, *supra,* at Ex. 29, p. 18.)

[12] In the interest of completeness I will briefly note that initially Dr. Latov proposed that anti-carbohydrate antibodies, which may be induced by the carbohydrate or polysaccharide chains derived from pneumococcus bacilli, can cross react with glycolipids or glycoproteins in normal tissue. (Ex. 46, pp. 1-2.) In a later report, however, Dr. Latov presented two alternatives that he then discussed during the hearing. One was the theory addressed in the analysis below. The other was based on his observation that studies relating to a different nervous system condition, Fabry disease, shows that a p-antigen (Ceramide trihexoside) is present in the peripheral nerves. (Ex. 56, p. 1 (citing A. Heilberg et al., *P1PK: The Blood Group System That Changed Its Name and Expanded,* 29 IMMUNOHEMATOLOGY 25 (2013) (Ex. 63); Soumeya Bekri et al., *The Role of Ceramide Trihexoside (Globotriaosylceramide) in the Diagnosis and Follow Up of the Efficacy of Treatment of Fabry Disease: A Review of the Literature*, 4 CARDIOVASCULAR & HEMATOLOGICAL AGENTS MED. CHEMISTRY 289 (2006) (Ex. 57)).) A separate study showed that anti-p antibodies have been shown to react with carbohydrates and glycosphingolipids on red blood cells. (*Id*. citing Hisako Hayashi et al., *Paroxysmal Cold Hemoglobinuria Caused by IgM-Class Donath-Landsteiner Antibody,* 55 PEDIATRIC INT'L 664 (2013) (Ex. 62)).) He suggests that this supports molecular mimicry between the pneumococcal coat polysaccharides and nerve oligosaccharides. (*Id.*)

Dr. Latov proposes that the potential for cross reaction between phosphate groups contained within the Prevnar vaccine and phospholipids within the peripheral nerves is demonstrated by several studies. (Ex. 56, p. 1.) First, he notes that the immunogenicity of the Prevnar vaccine depends on the attachment of the capsular polysaccharides to phoshoglyercol. (*Id*. (citing Janoi Chang et al., *Relevance of O-Acetyl and Phosphoglycerol Groups for the Antigenicity of* Streptococcus pneumoniae *Serotype 18C Capsular Polysaccharide,* 30 VACCINE 7090 (2012) (Ex. 59); Czeslaw Lugowski & Harold J. Jennings, *Structural Determination of the Capsular Polysaccharide of* Streptococcus pneumoniae *Type 18C (56),* 131CARBOHYDRATE RSCH. 119 (1984) (Ex. 66)).) Second, he explains that a study by Ho et al., examining a different demyelinating condition, multiple sclerosis, has demonstrated not only that phoshoglycerol is present in peripheral nerve myelin, but also that phospholipid antibodies bind to these tissues via the phosphate moieties.[13] (*Id.* (citing Peggy P. Ho et al., *Identification of Naturally Occurring Fatty Acids of the Myelin Sheath That Resolve Neuroinflammation,* 4 SCI. TRANSLATIONAL MED. 1 (2012) (Ex. 64)).) Two further studies have in turn shown that antibodies to phospholipids have been observed in actual patients with GBS. (*Id*. (citing B. Gilburd et al., *Autoantibodies to Phospholipids and Brain Extract in Patients with the Guillain Barré Syndrome: Cross Reactive or Pathogenic?,* 16 AUTOIMMUNITY 23 (1993) (Ex. 61); G. Nakos et al., *Anti-Phospholipid Antibodies in Serum from Patients with Guillain-Barré Syndrome,* 31 INTENSIVE CARE MED. 1401 (2005) (Ex. 67)).) Although neither of those studies concluded that the antiphospholipid antibodies were disease-causing among the GBS patients, the Gilburd study included some further evidence that the antibodies react to phosphatidic acid. (*Id*. (citing Gilburd et al., *supra,* at Ex. 61).) According to Dr. Latov, these studies collectively provide circumstantial evidence of cross-reactive potential because they show the phosphatidal groups to be both the immunogen in the vaccine and the target of immune reactivity in the myelin and further that the relevant antibodies for this proposed cross reaction are documented in actual patients with GBS. (Tr. 79-80.)

Dr. Latov acknowledges it would take a laboratory effort to actually prove this theory. (Tr. 100.) However, he asserts his opinion is based on reliable experimental evidence such that he opines that petitioner's vaccination more likely than not caused his GBS. (*Id.* at 80, 88.)

[13] The phosphate moiety refers to the part of the phosphoglycerol that contains phosphate, which would be the part of the phosphoglycerol that the phospholipid antibodies bind to. In chemistry, "a moiety is a part of a molecule that is given a name because it is identified as a part of other molecules as well." *Moiety (chemistry),* WIKIPEDIA, https://en.wikipedia.org/wiki/Moiety_(chemistry) (last visited March 8, 2024).

b. Respondent's Expert, Brian C. Callaghan, M.D., M.S.

Dr. Callaghan submitted four reports and also testified at the hearing, without objection, as an expert in neurology.[14] (Tr. 127.) Although Dr. Callaghan agrees that petitioner has suffered from GBS, he asserts that "the cause is unclear." (Ex. H, p. 1; *see also* Ex. A, p. 3.)

Dr. Callaghan explains that many GBS patients develop the condition without identification of any particular trigger. (Tr. 161.) Thus, he asserts that petitioner's GBS was more likely *not* caused by his vaccinations. (*Id.* at 132 (emphasis added).) Dr. Callaghan notes that none of petitioner's treating physicians attributed his GBS to his vaccinations in the medical records, beyond listing the vaccinations as a "risk factor" in one instance. (*Id.* at 130.) However, Dr. Callaghan explains that this one-off suspicion of vaccine causation was likely the result of the treating physician not entirely understanding the medical literature concerning vaccine-causation of GBS. (*Id.* at 130-31.) He asserts that a connection between Prevnar and GBS is not generally accepted in the neurological and medical community. (*Id.* at 132.)

Dr. Callaghan acknowledges that there is some epidemiologic literature in the form of case reports supporting a connection between the Prevnar vaccine and GBS but contends that "[t]here basically is a lack of data." (Tr. 133.) He agrees with petitioner's citation to the IOM's Immunization Safety Review insofar as the report found causal evidence linking the 1976 influenza vaccination and GBS; however, he stresses there is inadequate evidence linking post-1976 influenza vaccines with GBS. (Ex. A, p. 2 (citing INSTITUTE OF MEDICINE, IMMUNIZATION SAFETY REVIEW: INFLUENZA VACCINES AND NEUROLOGICAL COMPLICATIONS 44 (Stratton et al. eds., 2004) [hereinafter 2004 IOM review] (Ex. 36)).) The review also mentions that VAERS reports and case reports are uninformative for determining causation. (*Id.*; Ex. G, p. 1; *see also* Tr. 152-53.) In line with the IOM's apparent position that VAERS reports and case reports are not informative on the issue of causation, Dr. Callaghan contends the VAERS report and case report provided by Dr. Latov (Exhibits 32 and 39) are also uninformative. (Ex. A, p. 2.)

Dr. Callaghan cites one study that he posits disfavors any causal relationship between the Prevnar vaccine and GBS. (Ex. G, p. 1 (citing Penina Haber et al., *Post-Licensure Surveillance of 13-Valent Pneumococcal Conjugate Vaccine (PCV13) in*

[14] Dr. Callaghan received his medical degree from the University of Pennsylvania Medical Center and his Master of Science degree in clinical research design and statistical analysis from the University of Michigan. (Ex. B, p. 1.) He completed his residency in neurology at the university of Pennsylvania Medical Center. (*Id.*) Additionally, Dr. Callaghan completed a neuromuscular fellowship and a healthcare research and policy fellowship at the University of Michigan. (*Id.*) The neuromuscular fellowship provided "training specific to learning electrodiagnostics," such EMG and nerve conduction studies, as well as education on the nuances of seeing patients with neuromuscular disorders. (Tr. 122.) He currently serves as an associate professor of neurology at the University of Michigan and as a neuromuscular specialist at VA Ann Arbor Healthy System, with a primary interest in patients with neuropathy, such as GBS. (Ex. A, p. 1; Ex. B, 1.) Dr. Callaghan has treated more than 50 patients with GBS. (Ex. A, p. 1.) He has published more than 90 articles primarily focusing on neuropathy, including diagnostic evaluation and treatment. (*Id.*; Ex. B, pp. 10-17; Tr. 125.)

Adults Aged ≥ 19 Years Old in the United States, Vaccine Adverse Event Reporting System (VAERS), June 1, 2012-December 31, 2015, 34 VACCINE 6330 (2016) (Ex. C)).) While the Haber et al. paper did not include a control group, Dr. Callaghan contends that the data applies Bayesian data mining methods to evaluate whether VAERS reports of GBS after Prevnar vaccination were higher than expected by chance. (*Id.* (citing Haber et al., *supra,* at Ex. C); *see also* Tr. 151-53.) The authors concluded that GBS was not more commonly reported than expected by chance, which Dr. Callaghan opines is a much higher level of evidence than the VAERS data provided by petitioner. (Ex. G, p. 1 (citing Haber et al., *supra,* at Ex. C).) Although he argues that the Haber study "is the best epidemiologic study we have," he admits fthat "it is still based on VAERS reports and, you know, at a pretty low level of evidence." (Tr. 169.) Additionally, Dr. Callaghan addresses the Tseng et al. article filed by petitioner, and explains that it reveals fewer incidences of GBS than would be expected after Prevnar vaccination in adjusted analyses, which provides even more data supporting a lack of association between Prevnar vaccination and GBS. (Ex. G, p. 1 (citing Tseng et al., *supra,* at Ex. 37); Tr. 135-36.) He further explains that Tseng et al. utilized diagnostic codes from physicians, which he suggests are notoriously incorrect and make the article's results less compelling. (Tr. 136.)

While petitioner posits that molecular mimicry and bystander activation are potential mechanisms for vaccinations and GBS, Dr. Callaghan contends there is no evidence for these mechanisms in relation to Prevnar causing GBS. (Ex. A, p. 3; *see also* Tr. 133.) He stresses that petitioner has not provided any evidence that there is a protein sequence found in the Prevnar vaccine that is similar to a self-protein sequence that could support his hypothesis. (Ex. A, p. 3.) Furthermore, the IOM suggests that there is weak evidence supporting biologic mechanisms, including molecular mimicry and bystander activation, linking influenza vaccinations and GBS. (*Id.* (citing 2004 IOM review, *supra,* at Ex. 36).) Importantly, Dr. Callaghan opines there is even less evidence pertaining to these mechanisms in relation to Prevnar and GBS. (*Id.*) Dr. Callaghan explains that several steps must be taken to prove a link via molecular mimicry between a vaccine and a specific injury. (Tr. 140-41.) He asserts that not even the first step, *i.e.*, identification of homology or structure, has been completed with regards to Prevnar and GBS. (*Id.* at 140.) While Dr. Latov discusses *C. jejuni* and acute motor axonal neuropathy, Dr. Callaghan insists the relevance to Prevnar and AIDP is unclear. (*Id.* at 141-42; Ex. H, p. 1.) Dr. Callaghan raises further concern with petitioner's theory, explaining that petitioner had a typical demyelinating variant of GBS, not the axonal variant that is described by Caporale et al. (Ex. H, p. 1 (discussing Christina M. Caporale et al., *Experimental Axonopathy Induced by Immunization with* Campylobacter jejuni *Lipopolysaccharide from a Parent with Guillain Barrè Syndrome,* 174 J. NEUROIMMUNOLOGY 12 (2006) (Ex. 27)).) In response to Dr. Latov's contention that the Prevnar vaccine contains a causative immunostimulant, similar to pertussis, that can lead to experimental allergic encephalomyelitis, Dr. Callaghan opines that it is unclear whether there is any connection between Prevnar and pertussis or between EAE and GBS. (Ex. G, p. 1.)

Dr. Callaghan testified that the Gilburd study's results, which suggested that the production of autoantibodies was likely a result of myelin damages, rather than the cause of demyelination, show "how little we know about these antibodies and whether they have any role in the pathogenesis of GBS." (Tr. 146-47 (discussing Gilburd et al., *supra,* at Ex. 61, pp. 1, 6.) Dr. Latov opines that the Prevnar vaccine's capsular polysaccharides are attached via phosphoglycerol groups, and that these groups are also present in peripheral nerve myelin phospholipids, however, Dr. Callaghan contends there is no evidence demonstrating that the Prevnar vaccine leads to production of an immune response to phosphoglycerol groups (the main components of cell membranes in general) and/or that this immune response can lead to GBS specifically. (Ex. I, p. 1.) He further asserts that Dr. Latov's reliance on the article by Ho et al. is misplaced as multiple sclerosis and GBS are like "apples and orange." (Tr. 147-48 (discussing Ho et al., *supra,* at 64).) He explains that, while multiple sclerosis and GBS are both autoimmune conditions affecting myelin, they affect different nervous systems (central versus peripheral), they are pathologically distinct, they have different "triggers," they have different treatments, and one affects the brain and spinal cord while the other affects the peripheral nerves. (*Id.* (discussing Ho et al., *supra,* at Ex. 64).) Dr. Callaghan notes that the studies by Ho et al. and Nakos et al. were similarly limited to a finding that the antiphospholipid antibodies may be considered biomarkers of an existing autoimmune process, but there is not enough evidence to suggest that they are an instigating cause.[15] (*Id.* at 147-49 (discussing Ho et al., *supra,* at Ex. 64; Nakos et al., *supra,* at Ex. 67).)

Dr. Callaghan opines the timing of vaccination to onset of GBS does not show any evidence for a causal association. (Ex. A, p. 3; *see also* Tr. 153.) Petitioner relies on an article by Schonberger et al. to substantiate increased GBS even at 9 weeks after the 1976 flu vaccination. (Ex. A, p. 3 (citing Schonberger et al., *supra,* at Ex. 33).) However, Dr. Callaghan explains that Langmiur et al. subsequently re-analyzed those results and found that, when the only appropriate cases of GBS are included, the association between the 1976-77 swine flu vaccination and GBS only lasted for 6 weeks, and the rate of GBS fell back to baseline. (*Id.* (citing Langmuir et al., *supra,* at Ex. 43); Tr. 153-54.) The authors also point out that cases with limited involvement did not show a lognormal curve indicating no causal relationship, in contrast to those with more definitive GBS. (Ex. G, p. 1 (discussing Langmuir et al., *supra,* at Ex. 43).) Furthermore, the IOM reports that, by the 7th week, the rate of GBS fell back to baseline. (*Id.* at 2; Ex. A, p. 3 (discussing 2012 IOM Report, *supra,* at Ex. 29; 2004 IOM review, *supra,* at Ex. 36).) Dr. Callaghan observes that petitioner suffered GBS more than 8 weeks post vaccination, which is outside of this window—even if the subject vaccine was influenza. (Ex. A, p. 3.) Further, the vaccine injury table adopted this same time period of 3 days to 6 weeks as an acceptable time for any temporal

[15] Because I have limited discussion of Dr. Latov's theory to one of the three molecular mimics he proposed, I have similarly limited discussion of Dr. Callaghan's opinion to his responses to the operative aspect of Dr. Latov's opinion. Of course, Dr. Callaghan did provide responses to the other aspects of Dr. Latov's theory. Though not all aspects of Dr. Callaghan's opinion are explicitly discussed, I have been careful to evaluate Dr. Callaghan's opinion holistically.

correlation of GBS onset after influenza vaccination. (*Id.*) Ultimately, Dr. Callaghan opines petitioner suffered from GBS, but the cause is unclear. (*Id.*)

V. Discussion

a. *Althen* prong one

Under *Althen* prong one, petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Human Servs.,* 451 F.3d 1352, 1355-56 (Fed. Cir. 2006) (quoting *Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004)). Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen,* 35 F.3d at 548-49. Petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *See Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano v. Sec'y of Health & Human Servs.,* 440 F.3d 1317, 1325-26 (Fed. Cir. 2006)). However, "[a] petitioner must provide a 'reputable medical or scientific explanation' for [her] theory. While it does not require medical or scientific certainty, it must still be 'sound and reliable.'" *Boatmon,* 941 F.3d at 1359 (quoting *Knudsen*, 35 F.3d at 548-49).

As with many cases in the program, petitioner's theory involves molecular mimicry. Molecular mimicry is a concept with several constituent parts whereby (1) a susceptible host (2) encounters a foreign antigen has sufficient similarity ("homology") with components of host tissue such that (3) the immune system "cross reacts," producing antibodies that attack the host tissue instead of the foreign antigen to (4) ultimately cause disease or injury. (2012 IOM Report, *supra,* at Ex. 29, p. 17.) Molecular mimicry "is a generally accepted scientific principle, [but] mere invocation of the scientific term does not carry a petitioner's burden in a Program case." *Deshler v. Sec'y of Health & Human Servs*., No. 16-1070V, 2020 WL 4593162, at *20 (Fed. Cl. Spec. Mstr. July 1, 2020) (citing *Forrest v. Sec'y of Health & Human Servs.*, No. 14-1046V, 2019 WL 925495, at *3 (Fed. Cl. Spec. Mstr. Jan. 18, 2019)). This is because, as respondent's expert has stressed in this case (*see* ECF No. 86, pp. 10-11), "the finding of sequence homology does not necessarily mean the similarity has significance to the immune system." *Tullio v. Sec'y of Health & Human Servs.*, No. 15-51V, 2019 WL 7580149, at *15 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), ***aff'd,*** 149 Fed. Cl. 448 (2020); *see also Caredio v. Sec'y of Health & Human Servs.,* No. 17-0079V, 2021 WL 4100294, at *31 (Fed. Cl. Spec. Mstr. July 30, 2021) ("*demonstration of homology alone is not enough to establish a preponderant causation theory*") (emphasis in original) (citing *Schultz v. Sec'y of Health & Human Servs.,* No. 16-539V, 2020 WL 1039161, at *22 n. 24 (Fed. Cl. Spec. Mstr. Jan. 24, 2020), *mot. for rev. denied,* 2021 WL 6058835 (Fed. Cl. Dec. 3, 2021). However, as noted above, petitioners in this program are not required to establish scientific certainty. Therefore, prior cases have expressed with regard to the application of molecular mimicry that "[t]he line must be drawn somewhere between speculation and certainty." *Brayboy v. Sec'y of Health & Human Servs.,* No.

15-183V, 2021 WL 4453146, at *19 (Fed. Cl. Spec. Mstr. Aug. 30, 2021). Thus, for example, in *Brayboy*, an omnibus proceeding addressing autoimmune premature ovarian insufficiency, the special master found it sufficient that the petitioners "identified cross-reaction between components of the vaccine and proteins in the body that are directly responsible for the health and productivity of the organ at issue" and further expressed that requiring further steps, or insisting on direct, testable evidence, would impermissibly heighten the petitioners' burden of proof. *Id*.

In this case, Dr. Latov explains that, although the pathophysiology of GBS is incompletely understood, the current understanding of GBS provides some basic support for his opinion that the Prevnar vaccine can cause GBS. (*See* Ex. 42, pp. 1-2.) It is well established that GBS is an autoimmune condition affecting the peripheral nerves, most notably affecting the myelin tissue in the case of AIDP. (Ex. 23, p. 3; Tr. 51-53.) Although there is not epidemiologic evidence specifically linking s. pneumoniae to GBS (Tr. 142-43; Ex. 42, pp. 1-2), it is generally accepted that a number of different infectious antigens can cause GBS, including unspecified upper respiratory infections. (*See* Martin Arias et al., *Guillain-Barrè Syndrome and Influenza Vaccines: A Meta-Analysis,* 33 VACCINE 3773, 3773 (2015) (Ex. F, p. 1) ("GBS has been shown to be associated with antecedent gastrointestinal or upper respiratory tract infections, including influenza."); Israeli et al., *supra*, at Ex. 30, p. 1 ("Often, GBS occurs a few days or weeks after the patient has had symptoms of a respiratory or gastrointestinal microbial infection . . . About a third of all cases of [GBS] are preceded by *Campylobacter jejuni* infection.") This includes both viral and bacterial infections. (Israeli et al., *supra,* at Ex. 30, p. 3; *see also* Tr. 92, 96.) Additionally, for at least one of these antigens, *Campylobacter jenjuni*, there is sufficient proof to conclude that molecular mimicry is the mechanism of causation leading to GBS, albeit resulting primarily in the axonal subtype of GBS and involving a molecular mimic not at issue here. (2012 IOM Report, *supra,* at Ex. 29, p. 18-19; Tr. 173.) Evidence also supports homology between various other antigens and myelin tissue. (2012 IOM Report, *supra,* at Ex. 29, p. 18 (hepatitis B virus); Ex. 23, p. 4 (citing Applebaum et al., *supra*, at Ex. 25 (rabies).) In that regard, respondent's expert agrees that multiple antigens are implicated as causes of GBS and that we do not know the full scope of the antibodies that may be implicated in the pathology of GBS. (Tr. 138.) Further to this, a rabies vaccine has been identified as a cause of inflammatory neuropathies and at least some formulations of the flu vaccine have been identified as a cause of GBS in particular. (Tr. 95-96; Ex. 23, p. 3-4 (citing Appelbaum et al., *supra*, at Ex. 25; 2012 IOM Report, *supra,* at Ex. 29).) Without equating the flu vaccine and the Prevnar vaccine, Dr. Latov opines that broadly speaking this demonstrates that the immune response to vaccination, and not only active infection, is sufficient to cause GBS. (Tr. 95-96.)

In some prior cases, this background information has partly informed the special masters' analysis of a petitioner's theory of causation with respect to GBS. *E.g. J. G. v. Sec'y of Health & Human Servs.*, No. 20-664V, 2023 WL 2752634, at *30 (Fed. Cl. Spec. Mstr. Feb. 13, 2023) (observing that "[t]he experts do not dispute the theory of molecular mimicry, or that it is a sound and reliable theory generally as it relates to GBS" and that "[m]olecular mimicry has been accepted as a sound and reliable theory

in many Vaccine Program cases dealing with demyelinating conditions, including GBS."); *Osso v. Sec'y of Health & Human Servs.,* No. 18-575V, 2023 WL 5016473, at *21 (Fed. Cl. Spec. Mstr. July 13, 2023) (same); *Harris v. Sec'y of Health & Human Servs.,* No. 18-944V, 2023 WL 2583393, at *22 (Fed. Cl. Feb. 21, 2023) (finding that "the fact that GBS is well accepted as an autoimmune condition with a wide variety of suspected antigenic triggers, inclusive of antigens from both infection and vaccination, provides meaningful evidence supporting petitioner's burden of proof with respect to *Althen* prong one"); *but see Trollinger v. Sec'y of Health & Human Servs*., No. 16-473V, 2023 WL 2521912, at *30 (Fed. Cl. Spec. Mstr. Feb. 17, 2023) (finding that "Dr. Steinman's theory had a one-size-fits-all quality, in which he strained to shoehorn the science behind the flu-GBS association into the context of the pneumococcal vaccine" and further noting that "[i]f this were sufficient to establish that this particular vaccine 'can cause' GBS, it is hard to imagine the theory not also applying to *each and every one* of the sixteen Program-covered vaccines/vaccine antigenic components."(emphasis original)), *mot. rev. den'd* 167 Fed. Cl. 127 (2023). Although only the flu vaccine is presumed to be a cause of GBS in this program (42 C.F.R. §100.3(a)), petitioners have been found entitled to compensation in at least isolated instances for GBS caused by many other vaccines. This includes vaccines that target both viruses and bacteria. *See Salmins v. Sec'y of Health & Human Servs.*, No. 11-140V, 2014 WL 1569478 at *14 (Fed. Cl. Spec. Mstr. March 31, 2014) (finding the HPV vaccine "can cause" GBS); *Peugh v. Sec'y of Health and Human Servs.,* No. 99-638V, 2007 WL 1531666, at *17 (Fed. Cl. Spec. Mstr. May 8, 2007) (finding as part of an omnibus proceeding that hepatitis B vaccine can GBS); *Whitener v. Sec'y of Health & Human Servs.,* No. 06-0477V, 2009 WL 3007380, at *20 (Fed. Cl. Spec. Mstr. Sept. 2, 2009) (meningococcal vaccine found causal of GBS); *Koller v. Sec'y of Health & Human Servs.,* No. 16-439V, 2021 WL 5027947, at *7-20 (Fed. Cl. Spec. Mstr. Oct. 8, 2021) (finding pneumococcal conjugate vaccine can cause GBS); *Mohamad v. Sec'y of Health & Human Servs*., No. 16-1075V, 2022 WL 711604, at *9-18 (Fed. Cl. Spec. Mstr. Jan. 27, 2022) (finding Tdap vaccine can cause GBS); *J.G.,* 2023 WL 2752634, at *29-32 (finding Hep A vaccine can cause GBS). In fact, given the nature of the condition, molecular mimicry has been accepted as a theory of causation for GBS even in the absence of *any* demonstration of homology and cross-reaction. *Salmins*, 2014 WL 1569478, at *14.

Within that context Dr. Latov presents additional evidence to implicate the Prevnar vaccine in particular as a cause of GBS. This evidence includes a paper by Chang et al. which demonstrates that the Prevnar vaccine contains phosphoglycerol groups that are necessary to the vaccine's immunogenicity. (Tr. 74-75 (discussing Chang et al., *supra*, at Ex. 59).) Additionally, Dr. Latov cites an experimental study regarding a different demyelinating condition (multiple sclerosis) by Ho et al. Though primarily addressing potential anti-inflammatory possibilities of phospholipids, that study also demonstrated experimentally that the phosphate portion of phospholipid molecules has immune reactivity in the myelin tissue of the body. (*Id.* at 77-79 (discussing Ho, et al., *supra*, at Ex. 64, p. 4 (fig. 2(b) and 2(d)).) Further, Dr. Latov provides two studies that have shown that actual patients with GBS developed autoantibodies against phospholipids. (*Id.* at 75-77 (discussing Nakos, et al., *supra*, at Ex. 67; Gilburd, et al., *supra*, at Ex. 61).) Although the study authors did not reach a conclusion that these

antibodies were disease-causing, Dr. Latov explained of the Nakos, et al., study that "[p]hospholipids are often cross-reactive because of the phosphorous, which is so often the key antigen group, and they are reactive against several phospholipids, phosphotidylcholine, phosphotyidylnacetone, cardiolipin, [and] phospholipid acid. All these are present in the nerve tissue, and they were present, I think, in all of the Guillain-Barré patients and not in the controls." (*Id.* at 76.) Dr. Latov further asserts that the Gilburd, et al., study not only demonstrated the presence of these antibodies, but also demonstrated reactivity in at least some instances. (*Id.* at 77 (discussing Gilburd, *supra*, at Ex. 61, p. 4, Table 2).) Taken together, and given what we otherwise know about GBS, Dr. Latov opines that these studies demonstrate the cross-reactive potential necessary to invoke molecular mimicry between the Prevnar vaccine and myelin tissue. (*Id.* at 79.) That is, he explains that these studies show phosphatidyl groups to be both immunogenic as part of the vaccine and reactive in normal tissue, and, further, that the relevant autoantibodies have been shown to be present among patients with GBS. (*Id.*)

Although the studies Dr. Latov cites to link Prevnar and GBS have limitations, I find that Dr. Latov's opinion, supported both by these specific studies and the broader evidence regarding the causes of GBS, is sound and reliable and preponderantly supports a legally probable, though not scientifically certain, theory of causation sufficient to satisfy petitioner's burden of proof under *Althen* prong one. I reached the same conclusion in a prior case in which I discussed the details of these cited studies in greater depth. *Pierson v. Sec'y of Health & Human Servs.*, No. 17-1136V, 2022 WL 322836, at *27-31 (Fed. Cl. Spec. Mstr. Jan. 19, 2022). Additionally, other special masters have reached similar conclusions based on substantially similar underlying evidence. *Koller v. Sec'y of Health & Human Servs.*, No.16-439V, 2021 WL 5027947, at *16-20 (Fed. Cl. Spec. Mstr. Oct. 8, 2021) (Gowen); *Maloney v. Sec'y of Health & Human Servs*., No. 19-1713V, 2022 WL 1074087, at *30-32 (Fed. Cl. Spec. Mstr. Mar 17, 2022) (Dorsey); *Gross v. Sec'y of Health & Human Servs*., No. 17-1075V, 2022 WL 9669651, at *35-37 (Fed. Cl. Spec. Mstr. Sep. 22, 2022) (Dorsey); *Sprenger v. Sec'y of Health & Human Servs*., No. 18-279V, 2023 WL 8543435, at *18-20 (Fed. Cl. Spec. Mstr. Nov. 14, 2023) (Dorsey); *Parker v. Sec'y of Health & Human Servs.*, No. 20-411V, 2023 WL 9261248, at *20-22 (Fed. Cl. Spec. Mstr. Dec 20, 2023) (Dorsey); *Anderson v. Sec'y of Health & Human Servs.*, No. 18-484V, 2024 WL 557052 (Fed. Cl. Spec. Mstr. Jan. 17, 2024) (Dorsey); *see also Tracy v. Sec'y of Health & Human Servs*., No. 16-213V, 2022 WL 1125281, at *29-32 (Fed. Cl. Spec. Mstr. Mar. 30, 2022) (Special Master Sanders accepting a similar theory in the context of transverse myelitis).

Acceptance of this theory has not been unanimous among special masters. *Bialek v. Sec'y of Health & Human Servs*., 18-761V, 2023 WL 35509, at *33-37 (Fed. Cl. Spec. Mstr. Jan. 3, 2023) (Corcoran); *Trollinger*, 2023 WL 2521912, at *26-31 (Corcoran); *Gamboa-Avila v. Sec'y of Health & Human Servs*., No. 18-925V, 2023 WL 6536207 (Fed. Cl. Spec. Mstr. Sept. 11, 2023) (Corcoran), *mot. rev. den'd*, No.18-925V (Fed. Cl. filed Feb. 26, 2024).[16] However, these contrary decisions are not binding on

[16] Some additional cases were resolved against petitioners based on different theories of causation. *McConnell v. Sec'y of Health & Human Servs.*, No. 18-1051V, 2022 WL 4008238, at *7-9 (Aug. 19, 2022); *Deshler*, 2020 WL 4593162, at *19-21.

me. *Boatmon,* 941 F.3d at 1358-59; *Hanlon v. Sec'y of Health & Human Servs.,* 40 Fed. Cl. 625, 630 (1998). Nonetheless, I have considered the points raised by these decisions. I simply reach a different conclusion based on my overall weighing of the evidence on this record. Notably, even when reaching a different result, there has still been agreement that record evidence comparable to what has been presented in this case at a minimum

> *does* offer reliable support for the conclusion that phyosphoglycerol is found in the pneumococcal vaccine; that the immune system produces antibodies in reaction to the relevant antigens containing the phosphoglycerol; and that individuals with neuropathies (although some suffer from the distinguishable disease MS) have been shown in small sample studies to posses antibodies specific to myelin-containing phospholipids.

Trollinger, 2023 WL 2521912, at *28 (emphasis original).

Respondent stresses the distinction between the flu and pneumococcal vaccines. (ECF No. 86, p. 19-20.) Specifically, Dr. Callaghan asserted the pathophysiology of that vaccine is "quite different" from the Prevnar vaccine because one is directed toward a virus and the other is directed toward a bacterium. (Tr. 138-39.) However, Dr. Callaghan did not actually explain why this distinction is meaningful in itself. Moreover, he separately raised Campylobacter, a bacterium, as the prime example of a proven molecular mimic capable of causing GBS. (*E.g.*, *id.* at 141.) While Dr. Callaghan explained that Campylobacter is a distinct bacterium from the s. pneumoniae bacterium and results in a form of axonal GBS distinct from the demyelinating form of GBS (*Id.* at 141-42), the Campylobacter example still severely undercuts the notion that the difference between a virus and a bacterial target in itself represents any kind of bright line distinction vis-à-vis the potential causes of GBS. Dr. Callaghan otherwise acknowledges that there are multiple antibodies causally implicated in GBS and that we don't actually know the full range of them. (*Id.* at 138.) Moreover, as noted above, the literature filed in this case reflects that accepted causes of the demyelinating form of GBS includes both viral and bacterial illnesses. In that regard, Dr. Callaghan was careful to explain that we simply do not have the data needed to make that determination that s. pneumoniae is associated with GBS. (Tr. 143.) It is not the case that evidence exists to refute s. pneumoniae as a cause of GBS. As noted above, the GBS literature repeatedly references *unspecified* upper respiratory infections as being associated with GBS. Nor is it the case that Dr. Latov unreasonably conflates the flu and pneumococcal vaccines. In finding some significance in the fact that the flu vaccine can cause GBS, he was careful to explain that this observation related to the nature of GBS broadly and that he was not equating the two vaccines. (*Id.* at 95-97.)

Dr. Callaghan further raised that the Prevnar vaccine is designed to elicit a T-cell response whereas GBS disease process is primarily antibody mediated through a B-cell response. (Tr. 138.) While it is true that B-cells rather than T-Cells account for the production of autoantibodies (2012 IOM Report, *supra*, at Ex. 29, pp. 6-7), the B and T

Cell immune responses are *both* integral parts of the overall "array of reactions" that occur when the body encounters an antigen (*Id*. at 4-6). Despite raising this issue, Dr. Callaghan was himself careful to add that "nothing is pure B cell/T cell." (Tr. 138.) In that regard, the literature filed by petitioner indicates that GBS has been shown to include *both* demonstrated autoantibody and autoreactive T cells response. (Israeli et al., *supra*, at Ex. 30, p. 2.) Dr. Latov also explained that, while the pneumococcal conjugate vaccine receives a boost due to the T-cell response from the CRM 197 carrier protein contained in the vaccine, this is an adjuvant effect that is *additional* to the specific antigen response generated. (Tr. 79-80 (discussing Shinefield et al., *supra*, at Ex. 44).) Dr. Latov further explained that T-cell response itself contributes to the loss of self-tolerance that permits autoimmune disease to take effect. (Ex. 23, p. 4.) Thus, Dr. Latov invoked both molecular mimicry and bystander activation, specifically noting that the two mechanisms can operate in conjunction. (Tr. 60-61.) Accordingly, the distinction raised between B and T-cell responses does not meaningfully refute Dr. Latov's opinion.

Much of Dr. Callaghan's testimony consisted of isolated dismissals of each individual piece of petitioner's evidence because it is not *direct* evidence of a causal relationship between the Prevnar vaccine and GBS. However, a lack of *direct* supporting evidence does not render Dr. Latov's opinion either unsound or unreliable. Dr. Callaghan's observations are not inherently unreasonable; however, the Federal Circuit has stressed that requiring medical literature that is directly on point "contravenes section 300aa–13(a)(1)'s allowance of medical opinion as proof. This prevents the use of circumstantial evidence envisioned by the preponderance standard . . ." *Althen*, 418 F.3d at 1280 (citing *Knusden*, 35 F.3d at 549). Ultimately, Dr. Callaghan opines that what petitioner provides are only "first, first, first steps" in determining a causal relationship and that "there needs to be several other experiments afterwards to even starting thinking about what this means in the pathogenesis of GBS." (Tr. 145.) Dr. Callaghan asserts that "lots of holes" remain. (*Id.* at 146.) Importantly, however, what Dr. Callaghan is speaking to is scientific certainty (Tr. 139-40 (discussing Ex. 29, p. 17)), which is not petitioner's burden of proof. *Accord Sprenger*, 2023 WL 8543435, at *18 (rejecting respondent's expert's call to use the complete IOM criteria for assessing molecular mimicry as elevating petitioner's burden to scientific certainty). Notably, Dr. Callaghan does not assert that there is substantial evidence disfavoring petitioner's theory. Rather, he simply asserts that a good study of the type he envisions simply hasn't been done.[17] (Tr. 145-46.) "The standard of proof does not operate as a

[17] To be clear, upon further questioning by respondent's counsel, Dr. Callaghan was directly asked "[a]re there any studies you're are of that actually provide evidence weighing against Petitioner's theory in this case?" (Tr. 151.) He answered yes, and identified a single study by Haber, et al., which had previously been filed as Exhibit C. (*Id.* at. 151-53.) That study detected 0.7 cases of GBS per million doses of PCV13 vaccine administered. (Haber et al., supra, at Ex. C, p. 5.) Critically, however, the Haber study was based on a review of VAERS submissions. (*Id.*) Throughout his testimony, Dr. Callaghan was critical of the epidemiologic value of VAERS reports. In particular, he specifically endorsed language from the IOM as a "perfect description" of the value of VAERS reports. (Tr. 160 (discussing 2004 IOM review, *supra,* at Ex. 36, pp. 4-5).) That language specifically indicated that VAERS is a passive surveillance system for which, *inter alia*, underreporting and inadequate denominator data prevent its use to assess causality. (2004 IOM review, *supra,* at Ex. 36, pp. 4-5; *see also* Tr. 170.) Thus, Dr. Callaghan effectively minimizes his own reliance on the Haber study as reliable evidence disfavoring petitioner's

sliding scale that varies depending upon the quantity and quality of the scientific evidence that is available." *Caves v. Sec'y of Health & Human Servs*., 100 Fed. Cl. 119, 143 (2011), *aff'd*, 463 F. App'x 932 (Fed. Cir. 2012). However, evidence must be viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu*, 569 F.3d at 1380. The question ultimately is whether the alleged causal relationship is "legally probable, not medically or scientifically certain." *Id*. (quoting *Knudsen*, 35 F.3d at 548-49).) I have considered Dr. Callaghan's specific criticism and, while they may have the potential to carry significant weight in assessing scientific certainty, they are not dispositive under petitioner's legally probable burden of proof.

In light of all of the above, petitioner has satisfied *Althen* prong one by preponderant evidence.

b. *Althen* prong three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). In this case, both parties' experts frame their discussion of onset in reference to two seminal studies examining an outbreak of GBS following administration of the 1976 swine flu vaccine – Schonberger, et al., and Langmuir, et al. (Ex. 23, p. 4 (citing Schonberger et al., *supra*, at Ex. 33); Ex. A, p. 3 (citing Langmuir et al., *supra*, at Ex. E.)

Schonberger is an epidemiologic study evaluating over 1,000 individuals who were diagnosed with GBS in the 1976-77 timeframe. (Schonberger et al., *supra*, at Ex. 33.) Schonberger observed that the expected peak onset occurred 16 to 17 days post-vaccination (among the population of cases considered), though the majority of all GBS cases considered began within four weeks. (*Id.* at pp. 6-11.) However, Schonberger observed a statistically significant increase in reported cases as far out as nine to ten weeks post-vaccination. (*Id.* at pp. 1, 9.) Reexamining the same body of data from the same outbreak, but using a different case ascertainment and analysis, Langmuir concluded that "[t]he effect attributed to the vaccine lasted for at least six weeks and possibly for eight weeks but not longer." (Langmuir et al., *supra*, at Ex. E, p. 1.)

Dr. Latov discusses several reasons for preferring the Schonberger analysis over that of Langmuir. (Ex. 41, pp. 2-3 (discussing Langmuir et al., *supra,* at Ex. E).) First, he is critical of the Langmuir study for reducing the size of the examined population in

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theory. Even after having discussed the Haber study, Dr. Callaghan reiterated in concluding his direct examination that his critique of Dr. Latov's theory was "primarily a lack of data." (Tr. 161.) On cross-examination, he again noted that "there's actually really good epidemiologic study designs, which we don't really have here . . ." and specified the Haber study is "a pretty low level of evidence." (*Id.* at 165, 169.)

two ways. (*Id*.) He explains that 12.9% of patients were excluded to due to insufficient information despite having already been accepted by the CDC as cases of GBS. (*Id.* at 2.) This reduced the statistical significance of the vaccine effect. (*Id.*) The study also applied criteria for diagnosing GBS that was stricter than what is used in routine clinical practice. (*Id*. at 3.) Second, Langmuir compared the rate of GBS among the vaccinated population against rates reported in prior published studies from other regions and periods, rather than the corresponding unvaccinated population. (*Id*.) This again reduced the statistical significance of the vaccine effect by reflecting a higher background rate of GBS. (*Id*.) Dr. Latov explains that the study authors acknowledged the available unvaccinated data represented a larger population with "more statistical stability," but they felt the published studies had more thorough case ascertainment. However, Dr. Latov urged that the data set for the unvaccinated population rejected by the study authors was a better control because it utilized the same collection and screening process as the vaccinated population under study. (*Id*.) Additionally, according to Dr. Latov, the Langmuir study, notwithstanding the authors' analysis, includes data that shows elevated instances of GBS in weeks nine and ten post-vaccination. (*Id*. (citing Langmuir, *supra*, at Ex. E, p. 13 (Table 6); *see also* Tr. 105-07).)

Dr. Callaghan disagrees with Dr. Latov's critique and endorses the assumptions used by Langmuir. (Ex. G, pp. 1-2.) However, he noted during the hearing that "I'm not trying to be critical of Schonberger. I'm just saying the Langmuir group did it better, and I think, more importantly, the medical community agrees." (Tr. 179.) Thus, Dr. Callaghan contends the *maximum* allowable latency is the eight weeks identified by the Langmuir analysis. (*Id.* at 153-60; Ex. A, p. 3; Ex. G, pp. 1-2.) As petitioner's counsel addressed during cross-examination, Dr. Callaghan additionally submitted a much smaller study examining GBS within Ohio following the same vaccination. (Tr. 182-84 (discussing James S. Marks & Thomas J. Halpin, *Guillain-Barrè Syndrome in Recipients of A/New Jersey Influenza Vaccine,* 243 J. MED. ASS'N 2490 (1980) (Ex. D)).) It found a distribution similar to Schonberger. (*Id.*; Marks & Halpin, *supra*, at Ex. D, p. 2 (chart).) When prompted to observe that the Marks and Halpin study observed the same instances of GBS occurring during weeks four, five, seven, and ten, Dr. Callaghan observed that only small numbers were present and the real question is whether those numbers are above baseline. (Tr. 182-83.) However, Marks and Halpin are no more specific with respect to temporal association than to observe that it is significant that there was a clustering of cases within four weeks of vaccination. (Marks & Halpin, *supra*, at Ex. D, p. 4.) They note instead that "it is difficult to draw firm conclusions from the data developed here." (*Id*.)

Dr. Latov's criticisms do not convince me that the Schonberger study is superior or that the Langmuir study is deficient. Consistent with the Langmuir analysis, special masters have generally recognized eight weeks as the appropriate timeframe for onset of GBS. *E.g. Pierson*, 2022 WL 322836, at 32-38; *Barone v. Sec'y of Health & Human Servs.*, No.11-707V, 2014 WL 6834557, at * 13 (Fed. Cl. Spec. Mstr. Nov. 12, 2014). However, Dr. Latov does convince me that the Schonberger results cannot be entirely disregarded and that the Langmuir study, even though entitled to more weight, does not establish any hard and fast cut-off for the appropriate latency for vaccine-caused GBS

when considered as part of the record as a whole. For example, in a prior case in which petitioner's own expert had endorsed an eight-week latency period, I nonetheless noted that "[n]otwithstanding Langmuir's disagreement, there is some limited, albeit not preponderant, evidence from Schonberger to suggest onset could potentially exceed eight weeks." *Pierson*, 2022 WL 322836, at *33 n. 40.

Though there is a disagreement between the parties' experts regarding the comparative value of the Schonberger and Langmuir studies, these opinions are somewhat limited in that neither is an epidemiologist with the requisite training to fully parse the finer choices and assumptions of the studies' authors. Afterall, both studies are largely in agreement with regard to detecting an association between vaccination and GBS with the differences in analyses being significant only in relation to a minority of cases at the outer margin. Thus, for example, the IOM's 2004 report discussed the criticisms of the Schonberger study and compared it to the later Langmuir study, and then assessed the possible neurologic complications of the swine flu vaccine without entirely discounting the Schonberger findings, including the study as support for its finding that there is a causal relationship between the 1976 swine flu vaccine and GBS. (*See* 2004 IOM review, *supra,* at Ex. 36, p. 17.) Marks and Halpin, which was cited by Dr. Callaghan and also accounted for in the IOM's causal assessment regarding post-swine flu-vaccine GBS, declined to identify any overall risk period for post-vaccination GBS when looking at a similar, albeit smaller, data cluster. (Marks & Halpin, *supra*, at Ex. D; *see also* 2004 IOM review, *supra,* at Ex. 36, pp. 10-11, 24.)

As Dr. Callaghan noted during cross-examination regarding the IOM's critique of the Langmuir study, "there are limitations to every article . . ." (Tr. 181.) Given how close the latency in this case is to the proposed 56-day cut-off advanced by the Langmuir authors, *any* limitation of the Langmuir analysis, even if entirely reasonable, takes on increased importance. It is therefore worth observing, for example, that the Langmuir study examined statistical significance by 7-day increments. (Langmuir et al., *supra,* at Ex. E, p. 13 (Table 6).) Even taking Langmuir in isolation and assuming that all of the assumptions underlying the analysis were irrefutable, it would still not be clear that the analysis should be taken to reasonably conclude that 56-days, *but not one single day more*, is appropriate to infer causation. *Accord Paluck v. Sec'y of Health & Human Servs*., 786 F.3d 1373, 1383, 84 (Fed Cir. 2015) (finding that "[t]he special master further erred in setting a hard and fast deadline of three weeks between vaccination and the onset of clinically apparent symptoms of neurologic injury" where the studies of record "do not purport to establish any definitive timeframe for the onset of clinical symptoms . . .")

Regarding the facts of this case, both experts agree that petitioner's GBS first manifested on August 28, which is 60 days post-vaccination. (Tr. 103-04 (Dr. Latov); Tr. 153-54 (Dr. Callaghan).) Based on that latency, Dr. Latov, but not Dr. Callaghan, opines that vaccine causation can be inferred. (Ex. 23, p. 5; Ex. A, p. 3.) Consistent with Dr. Latov's opinion, petitioner's initial admitting physician, Dr. Santana, aware petitioner's prior vaccination occurred in June (*i.e*. about 60 or more days prior to onset of his GBS), nonetheless concluded that the vaccination was implicated as a "risk

factor" in bringing about his GBS. (Ex. 12, p 10.) The 60-day onset is within the outside limit as identified by Schonberger, but a mere four days beyond the eight-week timeframe stated by Langmuir. While the Langmuir analysis persuades me that vaccine causation should not be inferred for the full ten weeks identified by Schonberger, it is important to stress that the latency in this case is on the very edge of the entirely undisputed eight-week latency period and also has the support of petitioner's treating physician. *Accord Spayde v. Sec'y of Health & Human Servs*., No. 16-1499V, 2021 WL 686682, at *19 (Fed. Cl. Spec. Mstr. Jan. 27, 2021) (characterizing a 60-day onset of GBS "exceedingly close" to the accepted 56-day timeframe and indicating such onset would satisfy *Althen* prong three); *see also Althen*, 418 F.3d at 1280 (characterizing the Vaccine Program as a system in which "close calls regarding causation are resolved in favor of injury claimants.")

During the hearing Dr. Callaghan expressed skepticism regarding the degree of knowledge that most practicing physicians hold with regard to GBS, suggesting the relevant literature is not commonly reviewed. (Tr 130-31.) What Dr. Callaghan offers is a generic note of caution. On this record it is speculative when applied to Dr. Santana specifically. While treating physician opinions are not binding, treating physicians are considered well positioned to assess the sequence of cause and effect based on their patient's history and presentation. *Capizzano*, 440 F.3d at 1326. GBS is relatively rare (estimated incidences of up to about 2 cases per 100,000 individuals (Martin Arias et al., *supra,* at Ex. F, p. 1), but not so rare that blanket skepticism of any treating physician opinion is warranted. Dr. Santana's record does not suggest that she lacks familiarity with GBS. Both experts ultimately agree with the clinical diagnosis of GBS she rendered and her assessment evidences she is aware that GBS can be associated with a number of causes, including infectious causes, which she considered before identifying the vaccines as potentially significant. (Ex. 12, p. 10.)

Given the record as a whole, including both the Langmuir and Schonberger studies, the opinions of both parties' experts, and the admitting physician's assessment of the vaccine as a pertinent risk factor, I conclude that there is preponderant evidence that the 60-day period of onset in this case does allow an inference of vaccine causation. Petitioner has therefore satisfied *Althen* prong three by preponderant evidence.

c. *Althen* prong two

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant*, 956 F.2d at 1148. Medical records are generally viewed as particularly trustworthy evidence. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, medical records and/or statements of a treating physician's views do not *per se* bind the special master. *See* § 300aa-13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl.

706, 746 n. 67 (2009) ("there is nothing ... that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted.") A petitioner may support a cause-in-fact claim through either medical records or expert medical opinion. § 300aa-13(a). The special master is required to consider all the relevant evidence of record, draw plausible inferences and articulate a rational basis for the decision. *Winkler v. Sec'y of Health & Human Servs.,* 88 F.4th 958, 963 (Fed. Cir. 2023) (citing *Hines,* 940 F.2d at 1528).

In *Capizzano v. Secretary of Health and Human Services*, the Federal Circuit explained that:

> "A logical sequence of cause and effect" means what it sounds like—the claimant's theory of cause and effect must be logical . . . We see no reason why evidence used to satisfy one of the *Althen III* prongs cannot overlap to satisfy another prong. In other words, if close temporal proximity, combined with the finding that hepatitis B vaccine can cause RA, demonstrates that it is logical to conclude that the vaccine was the cause of the RA (the effect), then medical opinions to this effect are quite probative . . . We recognize, as the Court of Federal Claims observed, that the immense number of people receiving the hepatitis B vaccine statistically results in instances where individuals suffer an initial onset of rheumatoid arthritis shortly after receiving the vaccine, but not as the result of the vaccine. However, the statute requires only that the claimant show that it is more likely than not that *this claimant's* RA was caused by the vaccine.

440 F.3d at 1326 (emphasis original, internal citations omitted).[18]

The *Capizzano* Court reached its conclusion in light of the strength of treating physician opinions available in the case. 440 F. 3d at 1327-28. In later cases, the Federal Circuit indicated that "a petitioner is certainly permitted to use evidence eliminating other potential causes to help carry the burden on causation and may find it necessary to do so when the other evidence on causation is insufficient to make out a prima facie case." *Walther*, 485 F.3d at 1151 (citing *Pafford*, 451 F.3d 1352).

Here, petitioner's GBS diagnosis is undisputed. (Tr. 50-51 (Dr. Latov); Tr. 129-30 (Dr. Callaghan).) His expert, Dr. Latov, further opines that there is a logical

[18] On the other hand, the *Capizzano* Court also stated that:

> [t]he second prong of the *Althen III* test is not without meaning. There may well be a circumstance where it is found that a vaccine *can* cause the injury at issue and where the injury was temporally proximate to the vaccination, but it is illogical to conclude that the injury was actually caused by the vaccine. A claimant could satisfy the first and third prongs without satisfying the second prong when medical records and medical opinions do not suggest that the vaccine caused the injury, or where the probability of coincidence or another cause prevents the claimant from proving that the vaccine caused the injury by preponderant evidence.

440 F.3d at 1327 (emphasis original).

sequence of cause and effect supporting vaccine causation. (Tr. 81.) This is informed by several factors. (Ex. 23, p. 5.) As discussed separately under *Althen* prong three above, he persuasively opines that the timing of onset is appropriate for an inference of vaccine causation. (*See* V(b), *supra*; *see also Id*.) Electrodiagnostic studies confirmed demyelinating polyneuropathy. (*Id*. at 3.) Other possible causes of GBS were explored and ruled out. (*Id*. at 3, 5; Tr. 82.) Petitioner's admitting physician likewise opined that prior vaccination was the only possible risk factor for GBS implicated in petitioner's own case. (Ex. 12, p. 10; Tr. 81.) And, finally, petitioner had elevated CSF protein and his condition responded to IVIG treatment. (Ex. 23, p. 3.)

Respondent's expert, Dr. Callaghan, disagrees that the pneumococcal vaccine can cause GBS or that timing of onset in this case is appropriate to infer vaccine causation; however, these issues are addressed separately with respect to *Althen* prongs one and three. Dr. Callaghan has not otherwise presented any consideration that would additionally confound Dr. Latov's opinion regarding specific causation. Instead, he merely asserts that petitioner's GBS was idiopathic and that another cause is possible even if it cannot be identified. (Tr. 161, 184.) While Dr. Latov agrees GBS is often deemed idiopathic (*Id.* at 93), in this program a petitioner's claim is generally not defeated by that which is "idiopathic, unexplained, unknown, hypothetical, or undocumentable." § 300aa-13(a)(2); *Knudsen*, 35 F.3d at 547-48. That is, even as it is possible for a condition to be idiopathic, Dr. Callaghan's labeling it as such does not in itself provide any refutation of Dr. Latov's opinion.

In light of all of the above, petitioner has satisfied *Althen* prong two by preponderant evidence.

d. Factor unrelated

Once petitioner has satisfied his own burden of proof, respondent may demonstrate that the injury was caused by factors unrelated to vaccination. § 300aa-13(a)(1)(B); *Deribeaux v. Sec'y of Health & Human Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013). In this case, respondent has not offered any other factor as a potential cause of petitioner's GBS.

VI. Conclusion

After weighing the evidence of record within the context of this program, I find by preponderant evidence that petitioner suffered GBS caused-in-fact by the pneumococcal 13-valent conjugate vaccination he received on June 29, 2017. A separate damages order will be issued.

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master